AMENDMENTS

In the claims:

Please amend Claim 11 to read as follows.

1.(previously presented) An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1.

- 2. (original) An isolated nucleic acid molecule comprising a nucleotide sequence that:
 - (a) encodes the amino acid sequence shown in SEQ ID NO: 2; and
 - (b) hybridizes under stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof.
- 3.(original) An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO: 2.
- 4.(original) An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO:4.
 - 5. 10. (cancelled)
- 11.(currently amended) An expression vector comprising [a] <u>the</u> nucleic acid sequence of Claim 4.
 - 12.(previously presented) A cell comprising the expression vector of Claim 11.

RESPONSE

I. Status of the Claims

Claim 11 has been amended as suggested by the Examiner. Claims 1-4, 11 and 12 are pending .

II. Support for the Amended Claims

Amended Claim 11 finds support in original Claim 11 which found support in original Claim 4, throughout the specification as originally filed with particular support being found at least on page 13, lines 25-32.

As the amendments to Claim 11 are fully supported by the specification and claims as originally filed, they do not constitute new matter. Entry therefore is respectfully requested.

III. Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

Clam 11 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Although Applicants in no way agree, in order to further progress this application towards allowance, Claim 11 has been amended exactly as the Examiner requested and thus this rejection has been avoided and Applicants' therefore request its withdrawal.

IV. Rejection of Claims Under 35 U.S.C. § 101

The rejection of claims 1-4, 11-12 under 35 U.S.C. § 101 is maintained because the claimed invention allegedly is not supported by either a specific and substantial asserted utility or a well-established utility. This rejection is respectfully traversed, based on the following arguments as well as those presented in earlier responses.

The rejection of claims 1-4 is maintained in this Final Action which again asserts that Applicants have failed to identify the function of the protein encoded by the sequences of the present invention and that therefore there can be no specific, substantial or credible utility.

The Final Action dismisses Applicants' continued assertions that the protein of the present invention is a human semaphorin protein and that semaphorin protein function is both well known and implied to those of skill in the art. The Action at page 3, line 5, cites Bork (Genome Research 10:398-400, 2000) as supporting the proposition that prediction of protein function from homology information is somewhat unpredictable. However, a careful reading of Bork's publications and the other "relevant literature" does not in fact support the concept that function cannot be based on sequence and structural similarity, in contrast many of the examples actually support the use of such methodologies while identifying several areas in which caution should be exercised. These inaccuracies and potential pitfalls can be overcome by a more careful analysis by those of skill in the art. Automatic methods of sequence homology identification was only the staring point for consideration the sequences of the present invention underwent careful analysis by a series of individuals of skill in the art, many highly qualified (B.S. and Ph.D. level scientists).

These articles are merely examples of a small number of spurious publications that call into doubt the usefulness of bioinformatic predictions and that the PTO has repeatedly attempted to use as a basis to deny the utility of nucleic acid sequences. However, without going into the merits (or lack thereof) of all of the cited articles, Appellants point out that the lack of 100% unanimous agreement on the usefulness of bioinformatic prediction programs is completely irrelevant to the question of whether the claimed nucleic acid sequence has a substantial and specific utility. Appellants respectfully point out that the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be **believable**. Appellants submit that the overwhelming majority of those of skill in the relevant art would **believe** bioinformatic prediction to be a powerful and useful tool, as evidenced by hundreds if not thousands of journal articles.

Rather, the question of utility is a straightforward one. As set forth by the Federal Circuit, "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be <u>totally incapable</u> of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "<u>any</u> utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added.

Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable (*State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

As evidence of the credibility of Applicants assertion that the present invention is a variant of human semaphorin sem 2, In Applicants' response to the First Office Action (Paper No. 13) Applicants' submitted an amino acid sequence comparison between SEQ ID NO: 3 and BAA98132 (as Exhibit E), which was annotated by third party scientists, wholly unaffiliated with Applicants, as encoding semaphorin sem2 [Homo sapiens] (BAA98132: as Exhibit F). In this submission was included evidence that SEQ ID NO: 1 (see previously submitted Exhibit G comparing SEQ ID NOS: 3 and 1) identifies a longer isoform of the present invention, which is clearly encoded by the same genetic locus. Clearly those of skill in the art would recognize the sequences of the present invention as encoding a human semaphorin. As evidenced by the review article entitled "Molecular Mechanisms of Axonal Guidance" from the prestigious journal Science (298:1959-1964, 2002 and erratum; previously submitted as Exhibit H in Paper No. 13), semaphorins are well known to those of skill in the art as soluble and membrane-bound proteins that act as chemorepulsive factors in neuronal development, thereby playing a crucial role in axon guidance. Semaphorins, such as the one described in the present invention, provide guidance for neuronal growth. In the second paragraph of Section 5.1 or the specification as filed, it is stated that "Because of their role in neural development, semaphorins have been subject to considerable scientific scrutiny. For example, U.S. Patents Nos. 5,981,222 and 5,935,865, both of which are herein incorporated by reference, describe other semaphorins as well as applications, utilities". Therefore, clearly, there can be no question that Applicants' asserted identity and utility for the described sequences a semaphorin is "credible." In addition, those of skill in the art in the biomedical and pharmaceutical industry would readily recognize the utility for semaphorins and

their application to medical conditions requiring nerve regeneration. For example, the regeneration and repair of nerve tissue following the surgical attachment of severed limbs or the resection of diseased tissue, as well as nerve repair following a stroke.

Further support of Applicants' position that the function of the protein encoded by the sequences of the present invention is that of semaphorin sem 2 is further provided by the nucleotide sequence encoding the previously presented protein (BAA98132) shares 99.957 % percent homology over the entire nucleic acid sequence of SEQ ID NO:3 (nucleic acid alignment presented as New Exhibit AA; GenBank accession number AB029496).

Applicants have thus supplied evidence supporting their assertion that those of skill in the art would recognize that the sequences of the present invention encode variants of human semaphorin. Applicant's assertion also supports a "well-established" utility in that persons of ordinary skill in the art would immediately appreciate. In contrast, the Examiner has provided no evidence of record indicating that those of skill in the art would not recognize the sequences of the present invention encode semaphorin. As such, the scientific evidence clearly establishes that Applicants have described an invention whose utility is in full compliance with the provisions of 35 U.S.C. § 101, and therefore Applicants respectfully request withdrawal of the rejection.

The Final Action states that there is no disclosure in the specification suggesting that the sequences of the present invention as encoding the biological activity of human semaphorins (page 3 lines 9-10). However, the application clearly identifies similarities between the sequences of the present invention (SEQ ID NOS: 1-5) and semaphorin proteins (at least on page 2, lines 14-15; page 4, lines 10-11 and page 17, line 10) and their tissue expression distribution (page 4, lines 10-15) and describes the activity of semaphorins (page 4, lines 10-15) and well-established utility "Because of their role in neural development, semaphorins have been subject to considerable scientific scrutiny. For example, U.S. Patents Nos. 5,981,222 and 5,935,865, both of which are herein incorporated by reference, describe other semaphorins as well as applications, utilities, and uses ..." (page 17, lines 14-18). Clearly Applicants were aware at the time of filing of the semaphorin like nature of the protein encoded by sequences of the present invention.

Furthermore the Examiner's position that mere homology of SEQ ID No:1 to a known DNA molecule with a known function does not endow SEQ ID NO:1 with the function is contrary to Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials (pages 53-55), which

establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when there is no reason to doubt the asserted utility of a full length sequence (such as the presently claimed sequence) that has a similarity score of 95% to a protein having a known function. In the Analysis portion of Example 10 it states that "Based on applicant's disclosure and the results of the PTO search, there is no reason to doubt the assertion that SEQ ID NO:2 encodes a DNA ligase. Further DNA ligases have a well-established use in the molecular biology art based on this class of proteins ability to ligate DNA.Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed...... Thus the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be made."

The present case is similar to that presented in Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55). In the present case it is clear that the sequences of the present invention encode a semaphorin. Semaphorins have a well-established function. Thus a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not have been made and should therefore, be withdrawn.

As set forth in In re Langer (183 USPQ 288 (CCPA 1974); "Langer"):

As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented <u>must</u> be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter <u>unless</u> there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

Langer at 297, emphasis in original. As set forth in the MPEP, "Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered 'false' by a person of ordinary skill in the art" (MPEP, Eighth Edition at 2100-40, emphasis added). Thus, absent such evidence from the Examiner concerning the role of the presently claimed sequence encodes a protein kinase, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Action also disregards Applicant's asserted utility of the presently claimed polynucleotides on DNA chips (Action at page 3, Section 4.(ii)). Further, the Action seems to be requiring Applicants to identify the biological role of the nucleic acid or function of the protein encoded by the presently claimed polynucleotides before the present sequences can be used in gene chip applications that meet

the requirements of § 101. Applicants respectfully point out that knowledge of the exact function or role of the presently claimed sequence is not required to track expression patterns using a DNA chip. Given the widespread utility of such "gene chip" methods using public domain gene sequence information, there can be little doubt that the use of the presently described novel sequences would have great utility in such DNA chip applications. Particularly as Applicants have identified the protein encoded as a semaphorin, identified the specific tissues in which this gene is expressed (page 4, lines 10-15) and identified a specific polymorphism in SEQ ID NO:1 (page 17, lines 8-18). The claimed sequence provides a specific marker of the human genome (see evidence below), and that such specific markers are targets for discovering drugs that are associated with human disease. Thus, those skilled in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips, as the specification details. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, as well as more recently issued U.S. Patent Nos. 5,837,832, 6,156,501 and 6,261,776. Accordingly, the present sequence has a specific utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequence, must also be useful.

Additionally, since only a small percentage of the genome (2-4%) actually encodes exons, which in-turn encode amino acid sequences. Thus, not all human genomic DNA sequences are useful in such gene chip applications. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101. It has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971).

Evidence of the "real world" <u>substantial</u> utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company, Rosetta Inpharmatics, was viewed to have such "real world" value that it was acquired by large pharmaceutical company, Merck & Co., for substantial

sums of money (net equity value of the transaction was \$620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, e.g., Venter et al., 2001, Science 291:1304). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, e.g., Jasny and Kennedy, 2001, Science 291:1153). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years). The use of the claimed polypeptide in an array for screening purposes Applicants respectfully point out that nucleic acid sequences have the greatest specific utility in gene chip applications once the role of the sequence has been identified, as have tissues of interest, as in the present case. Once the role of the particular nucleic acid is known, the level of gene expression has and even greater significance. By identifying the physiological activity role of the claimed sequence, the claimed sequence has a far greater utility in gene chip applications that just any random piece of DNA.

As a still further example of utility is the use of the present sequences in such diagnostic assays (at least at page 9, line 7; page 18 line 11; page 25, line 32) as those associated with identification of paternity and forensic analysis, among others. The sequences of the present invention have particular utility as the application as filed identified a polymorphism in SEQ ID NO:1 (page 17, lines 8-18). This is also not a case of a potential utility. Appellants respectfully submit that even in the worst case scenario, the described polymorphisms are each useful to distinguish 50% of the population (in other words, the marker being present in half of the population) and that the ability of a polymorphic marker to distinguish at least 50% of the population is an inherent feature of any polymorphic marker, and this feature is well understood by those of skill in the art. Appellants note that as a matter of law, it is well settled that a patent need not disclose what is well known in the art. In re Wands, 8 USPQ 2d 1400 (Fed. Cir. 1988). Appellants support for Appellants' assertion of utility is provided by the fact that the skilled artisan would readily recognize and easily believe that the presently described polymorphic markers could be useful in forensic analysis. The fact that forensic biologists use polymorphic markers

such as those described by Appellants <u>every day</u> provides more that ample support for the assertion that forensic biologists would also be able to use the specific polymorphic markers described by Appellants in the same fashion. Therefore, again it is clear that the sequences of the present invention have utility.

Applicants respectfully submit that <u>specific</u> utility, which is the proper standard for utility under 35 U.S.C. § 101, is distinct from the requirement for a <u>unique</u> utility, which is clearly an <u>improper</u> standard. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; "*Carl Zeiss*"):

An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Therefore, just because other nucleic acid sequences find utility in gene chip applications does not mean that the use of Applicants' sequence in gene chip applications is not a specific utility. Furthermore, the requirement for a unique utility is clearly not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer and bacterial or viral infections, just to name a few particular examples, because examples of each of these have already been described and patented. All batteries have the exact same utility - specifically, to provide power. All automobile tires have the exact same utility - specifically, for use on automobiles. All golf balls and golf clubs have the exact same utility specifically, use in the game of golf. All cancer treatments have the exact same utility - specifically, to treat cancer. All anti-infectious agents have the exact same broader utility - specifically, to treat infections. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

The Action further discounts the utility of the claimed sequence for exon mapping as there is "no knowledge of what the function of the actual sequence, regardless of the basis of homology, then there is no asserted utility" (Final Action Page 4, line 4-6). Applicants respectfully submit that the function of the sequence as a semaphorin and several utilities were asserted in the application as filed (addressed above).

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (Raytheon v. Roper, 220 USPQ 592 (Fed. Cir. 1983); In re Gottlieb, 140 USPQ 665 (CCPA 1964); In re Malachowski, 189 USPQ 432 (CCPA 1976); Hoffman v. Klaus, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotides, as described in the specification at least at page 12 lines 4-10, the present nucleotide sequence has a specific utility in determining the genomic structure of the corresponding human chromosome, for example mapping the protein encoding regions. As evidence supporting Applicants assertions of the specific utility of the sequences of the present invention in localizing the specific region of the human chromosome and identification of functionally active intron/exon splice junctions is the information provided as Exhibit BB. This is the result of overlaying the sequence of SEQ ID NO:1 of the present invention and the identified human genomic sequence. By doing this, one is able to identify the portions of the genome that encode the present invention. As these regions of the genome are non-contiguous, this is indicative of individual exons. The results of such an analysis indicate that the sequence of the present invention is the result of a 16 exon gene contained within the BAC clone AC006208.3. Clearly as the gene of the present invention is encoded by 16 non-contiguous exons on chromosome 3, one would not have been able to deduce the sequence that encodes the molecules of the present invention without knowing the sequence. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 3 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful.

Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the

human genome, such as the present nucleic acid sequence. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Equally significant is that the claimed polynucleotide sequences define how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The presently claimed sequence clearly identified the intron/exon boundaries, as described above. The specification details that "sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (*e.g.*, splice acceptor and/or donor sites), *etc.*, that can be used in diagnostics and pharmacogenomics" (specification at page 8, lines 14-20). Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Applicants again draw attention to the distinction between the requirements of a <u>specific</u> utility with a <u>unique</u> utility. The fact that a <u>small number</u> of other nucleotide sequences could be used to map the protein coding regions in this <u>specific</u> region of chromosome 3 does not mean that the use of Applicants' sequence to map the protein coding regions of chromosome 3 is not a <u>specific</u> utility (*Carl Zeiss Stiftung v. Renishaw PLC*, *supra*).

Finally, while Applicants are well aware of the new Utility Guidelines set forth by the USPTO, it has been long established that the current rules regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants point out that guidelines that are not consistent with the patent laws, or the interpretation of these laws by the judicial branch, are not the final word in determining whether or not claims comply with any particular section of the patent laws. Applicants are unaware of any significant-recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claim short polynucleotides), none of which contain examples of the "real-world" utilities that

seem to be required in the Action. As issued U.S. Patents are presumed to meet <u>all</u> of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section III, below), Applicants submit that the presently claimed polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants understand that each patent application is examined on the basis of its individual merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. The requirement of Applicants to meet a <u>different</u> standard of utility in the present case would be arbitrary and capricious, and cannot stand.

In summary, the present situation is similar to Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when the full length sequence of the invention encodes a protein that has a well known function. Furthermore this response has described a series of additional substantial, specific, credible and well-established utilities for the present invention in addition to those described in Applicants' many previous responses. Therefore, Applicants submit that as the presently claimed sequence molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of the claims under 35 U.S.C. § 101 has been overcome. Thus, Applicants respectfully request that the rejection be withdrawn.

V. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

Claims 1-4, 11-12 are also rejected under 35 U.S.C. § 112 first paragraph. Specifically, since the claimed invention is not supported by either specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicants submit that all claims have been shown to have "a specific, substantial, and credible utility", as detailed above. Applicants therefore request that the rejection of all claims under 35 U.S.C. § 112, first paragraph, be withdrawn.

VI. Rejection of Claims Under 35 U.S.C. § 101 & 35 U.S.C. § 112

Claims 11-12 are rejected under the above 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, allegedly based on the same reasoning as above. As claims 11 and 12 are dependent upon Claim 4 and Claim 4 has now been shown to have a patentable utility under 35 U.S.C. Sections 101 and 112, this rejection has been avoided and Applicants, therefore, request withdrawal of the rejection.

VII. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Chism have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

September 22, 2003

Date

Lance K Ishimoto

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Customer # 24231

Exhibit AA

Page 1 of 5
RECEIVED
SEP 30 700

FASTA searches a protein or DNA sequence data bank version 3.3t05 March 30, 2000
Please cite:
W.R. Pearson & D.J. Lipman PNAS (1988) 85:2444-2448

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4700 residues in 1 sequences FASTA (3.34 January 2000) function [optimized, +5/-4 matrix (5:-4)] ktup: 6 join: 74, opt: 59, gap-pen: -16/ -4, width: 16 Scan time: 0.100 The best scores are: opt gi|8978201|dbj|AB029496.1| Homo sapiens mRNA f (4700) [f] 11742 gi|8978201|dbj|AB029496.1| Homo sapiens mRNA f (4700) [r] >>gi|8978201|dbj|AB029496.1| Homo sapiens mRNA for semap initn: 11742 init1: 11742 opt: 11742 99.957% identity in 2349 nt overlap (1-2349:1-2349) LEX151 ATGGCCCCTCGGCCTGGGCCATTTGCTGGCTGCTAGGGGGCCTCCTGCTCCATGGGGGT gi|897 ATGGCCCCTCGGCCTGGGCCATTTGCTGGCTGCTAGGGGGCCTCCTGCTCCATGGGGGT LEX151 AGCTCTGGCCCCAGCCCCGGCCCCAGTGTGCCCCGCCTGCGGCTCTCCTACCGAGACCTC gi | 897 AGCTCTGGCCCCAGCCCCGGCCCCAGTGTGCCCCGCCTGCGGCTCTCCTACCGAGACCTC LEX151 CTGTCTGCCAACCGCTCTGCCATCTTTCTGGGCCCCCAGGGCTCCCTGAACCTCCAGGCC gi | 897 CTGTCTGCCAACCGCTCTGCCATCTTTCTGGGCCCCCAGGGCTCCCTGAACCTCCAGGCC 130 . gi|897 ATGTACCTAGATGAGTACCGAGACCGCCTCTTTCTGGGTGGCCTGGACGCCCTCTACTCT LEX151 CTGCGGCTGGACCAGGCATGCCAGATCCCCGGGAGGTCCTGTGGCCACCGCAGCCAGGA gi|897 CTGCGGCTGGACCAGGCATGGCCAGATCCCCGGGAGGTCCTGTGGCCACCGCAGCCAGGA LEX151 CAGAGGGAGGGGTGTGTTCGAAAGGGAAGAGATCCTTTGACAGAGTGCGCCAACTTCGTG gi|897 CAGAGGGAGGAGTGTGTTCGAAAGGGAAGAGATCCTTTGACAGAGTGCGCCAACTTCGTG

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						::::::::		
	gi 897					CCTGAGAACT		
			670	680	690	700	710	720
•		•	730	740	750	760	770	780
	LEX151					TCGCCCGATG		
						:::::::::		
	gi 897					TCGCCCGATG		
	•		730 ·	740	750	760	770	780
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	LEXT51					GATGCTGGGG		
	ai 997					:::::::: GATGCTGGGG		
	giloji			800	810	820	830	840
			,,,,	000	810	820	630	040
		8	350	860	870	880	890	900
	LEX151	GTGAACA	AATGGAGCAC	TTTCCTCAAG	GCCAGGCTG	GTCTGCTCGG ^e	TGCCCGGCCC	TGGT
						:::::::::		
	gi 897					GTCTGCTCGG ⁽		
		8	350	860	870	880	890	900
		c	910	920	930	940	950	960
	LEX151					TTCCTGCTGT(
	- '					::::::::::		
	gi 897					TTCCTGCTGT		
	•				930	940	950	960
		_					•	
		9	970	980	9,90	1000	1010	1020

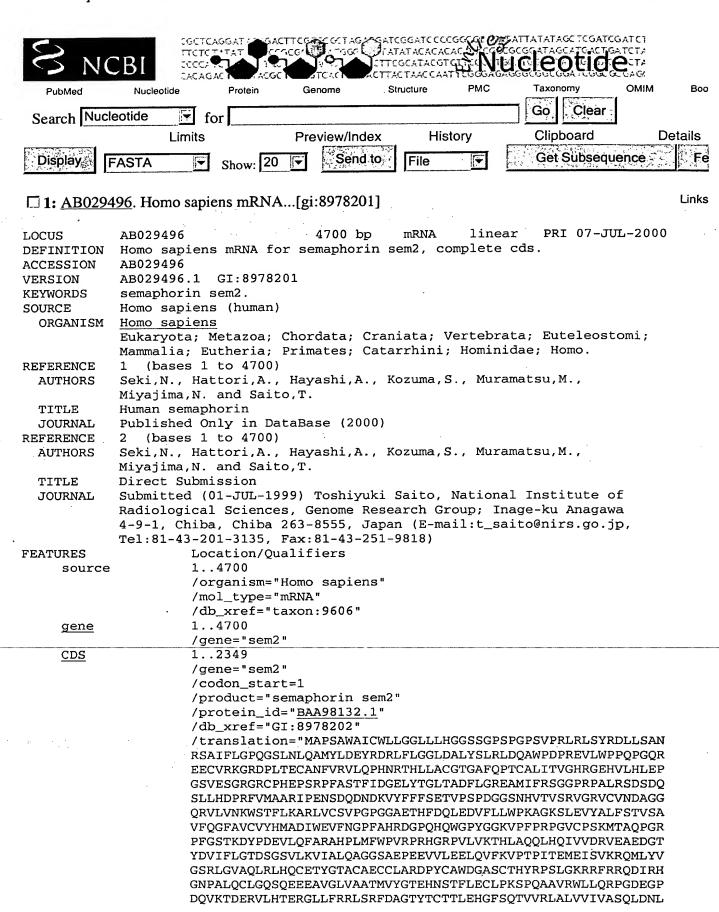
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gi 897	AAGAGC				TCAGTGCCGT		
		970	980	990	1000	1010	1020
		1030	1040	1050	1060	1070	1080
LEX151	GTCTGT				TTTTCAACGG(
					::::::::::		
gi 897	GTCTGT	GTGTACCAC	ATGGCAGAC	ATCTGGGAGG'	TTTTCAACGG	CCCTTTGCCC	CACCGA
		1030	1040	1050	1060	1070	1080
		1090	1100		1120	1130	1140
LEX151					GCAAGGTGCCC		
ai 1997					::::::::: GCAAGGTGCCC		
91 03 /	GAIGGG	1090	1100		1120	1130	1140
		1030	1100	1110	1120	1130	1140
		1150	1160	1170	1180	1190	1200
LEX151	GTGTGC	CCCAGCAAG	ATGACCGCAC	CAGCCAGGAC	GCCTTTTGGC	AGCACCAAGG	ACTAC
					: : : : : : : : : :		
gi 897	GTGTGC	CCCAGCAAG			GCCTTTTGGC	AGCACCAAGG	ACTAC
		1150	1160	1170	1180	1190	1200
		1010	1000	1000	1010	1050	
T EV151	CCACAM	1210	1220	1230	1240 CCTCATGTTC	1250	1260
PEYIOT					CCTCATGTTC		
gi 897					CCTCATGTTC		
3-1		1210		1230	1240	1250	1260
				8			
		1270	1280	1290	1300	1310	1320
LEX151					GGCCCAGCAG		
g1 897					'GGCCCAGCAG		
		1270	1280	1290	1300	1310	1320
		1330	1340	1350	1360	1370	1380
LEX151					TGTCATTTTC		
					::::::::		
gi 897	GTGGAC	CGCGTGGAGG	CAGAGGATG	GGACCTACGA	TGTCATTTTC	CTGGGGACTG	ACTCA
		1330 ·	1340	1350	1360	1370	1380
		1200	1400	1410	1.400	1 4 2 0	
-T-FY1-5-1		1390 Этсстсалас	1400	1410	1420 GGGCTCAGCT	1430	1440
DUMIJI					:::::::::		
gi 897	GGGTCT	GTGCTCAAAG	TCATCGCTC	TCCAGGCAGG	GGGCTCAGCT	GAACCTGAGG	AAGTG
- ,		1390	1400	1410	1420	1430	1440
		1450	1460	1470	1480	1490	1500
LEX151					ACCTATCACC		
					:::::::::::::::::::::::::::::::::::::::		
g1 89/		JAGGAGCTCC L450	AGGTGTTTA 1460	AGGTGCCAAC. 1470	ACCTATCACCO		
	_	1450	1460	14/0	1480	1490	1500
	1	510	1520	1530	1540	1550	1560
LEX151					GGGTGTGGCCC		
	::::::	:::::::::	::::::::	: : : : : : : : :			::::
gi 897	GTCAAAA	GGCAAATGC	TATACGTGG	GCTCTCGGCT	GGGTGTGGCCC	AGCTGCGGCT	GCAC
	1	510	1520	1530	1540	1550	1560
		570	1500	1500	1600	1.510	
	1	.570	1580	1590	1600	1610	1620

LEX15	1 CAATGTGAGACTT	ነ <u>ል</u> ርርርር ልርጥርር	'''''''''''''''''''''''''''''''''''''	ᢉ᠇ᡏᢗ᠊ᢗ᠇ᡏᢗ᠊ᢗᢁᢗ		7 A M A C M C M
DDMIS	:::::::::::					
gi 89	7 CAATGTGAGACTT	ACGGCACTGC	CTGTGCAGA	GTGCTGCCTG(GCCCGGGACCC	CATACTGT
	1570	1580	1590	1600	1610	1620
	1630	1640	1650		1670	1680
LEX15	1 GCCTGGGATGGTG					
gi 89	::::::::::::::::::::::::::::::::::::::	CCTCCTGTAC	CCACTACCG	CCCCAGCCTT	GCAAGCGCCG	GTTCCGC
	1630	1640	1650	1660	1670	1680
	1690	1700	1710	1720	1730	1740
LEX15	L CGGCAGGACATCC					
	:::::::::::::::::::::::::::::::::::::::	::::::::::	::::::::::	::::::::::	::::::::::	::::::
g1 89 .	7 CGGCAGGACATCC	GGCACGGCAA 1700	CCCTGCCCTG 1710	CAGTGCCTGG 1720	GCCAGAGCCA 1730	GGAAGAA 1740
		1.00	1710	1720	1750	1/40
T PV1 E 1	1750		1770	1780	1790	1800
PEVIO	GAGGCAGTGGGACT					
gi 897	GAGGCAGTGGGACT	TTGTGGCAGC	CACCATGGTC	TACGGCACGG	AGCACAATAG	CACCTTC
	1750	1760	1770	1780	1790	1800
	1810	1820	1830	1840	1850	1860
LEX151	CTGGAGTGCCTGCC	CAAGTCTCC	CCARGCTGCT	GTGCGCTGGC	TCTTGCAGAG	GCCAGGG
ai 897	::::::::::::::::::::::::::::::::::::::	CA A CTCTCTCC	:::::::::	:::::::::	:::::::::	::::::
911057	CTGGAGTGCCTGCC 1810	1820	1830	GIGCGCIGGC 1840	TCTTGCAGAG(1850	GCCAGGG 1860
	0				2000	1000
LEX151	1870 GATGAGGGGCCTGA	1880 .CCACGTGAAC	1890	1900	1910	1920
	:::::::::::::::::::::::::::::::::::::::	:::::::::		: : : : : : : : :	: : : : : : : : : :	
gi 897	GATGAGGGGCCTGA	CCAGGTGAAC	SACGGACGAG	CGAGTCTTGC	ACACGGAGCG	GGGCTG
	1870	1880	1890	1900	1910	1920
	1930	1940			1970	1980
LEX151	CTGTTCCGCAGGCT					
gi 897	CTGTTCCGCAGGCT	::::::::::::::::::::::::::::::::::::	::::::::::::::::::::::::::::::::::::::	::::::::::::::::::::::::::::::::::::::	::::::::::::::::::::::::::::::::::::::	::::::
- •	1930	1940	1950	1960	1970	1980
	1990	2000	2010	2020	2020	
LEX151	GGCTTCTCCCAGAC		CTGGCTCTGC	2020 TGGTGATTGT	2030	2040 CTGGAC
	:::::::::::::::::::::::::::::::::::::::	::::::::::	::::::::::	::::::::::		
91 09/	GGCTTCTCCCAGAC'	TGTGGTCCGC 2000	CTGGCTCTGG	TGGTGATTGT 2020	'GGCCTCACAG 2030	
			2010	2020	2030	2040
T.EV151	2050	2060	2070	2080	2090	2100
DEXIC	AACÇTGTTCCCTCCC	GAGCCAAAG	CCAGAGGAGC	CCCCAGCCCG	GGGAGGCCTG	GCTTCC
gi 897	AACCTGTTCCCTCC(GGAGCCAAAG	CCAGAGGAGC	CCCCAGCCCG	GGGAGGCCTG	GCTTCC
	2050	2060	2070	2080	2090	2100
	2110	2120	2130	2140	2150	2160
LEX151	ACCCCACCCAAGGCC	CTGGTACAAG	GACATCCTGC	AGCTCATTGG	CTTCGCCAAC	CTGCCC
gi 897	ACCCCACCCAAGGCC	**************************************	::::::::::::::::::::::::::::::::::::::	::::::::::::::::::::::::::::::::::::::	::::::::	:::::
J=155,	2110	2120	2130	AGCTCATTGG 2140	CTTCGCCAAC(2150	CTGCCC 2160
	0150	0.1.0.0	04.6-5		•	
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      gi|897 CGGGTGGATGAGTACTGTGAGCGCGTGTGGTGCAGGGGCACCACGGAATGCTCAGGCTGC
                                                       2220
                                     2200
                                              2210
           2170
                    2180
                             2190
                                              2270
                             2250
                                     2260
                    2240
           2230
LEX151 TTCCGGAGCCGGAGCCGGGCAAGCAGGCCAGGGCAAGAGCTGGGCAGGGCTGGAGCTA
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                    2240
                             2250
                                     2260
           2230
                                                       2340
            2290
                    2300
                             2310
                                     2320
                                              2330
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                                              2330
                                     2320
LEX151 GCCACGTAG
      :::::::
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                                     2380
                                              2390
                                                       2400
                             2370
           2350
                    2360
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         900
                 890
                          880
                                   870
                                           860
                                                    850
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                 460
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         840
LEX15- TTCACCAGCACCCGCTGGCCCCCAGCATCATTCACGCAGACGCGGCCCACGCGGCTGACA
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<u>Disclaimer | Write to the Help Desk</u> <u>NCBI | NLM | NIH</u>

Sep 4 2003 10:24:36

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FASTA searches a protein or DNA sequence data bank
 version 3.3t05 March 30, 2000
Please cite:
W.R. Pearson & D.J. Lipman PNAS (1988) 85:2444-2448
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The best scores are:
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gi|897
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            320
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LEX151 CTGCTAGGGGGCCTCCTGCTCCATGGGGGTAGCTCTGGCCCCAGCCCCGGCCCCAGTGTG
     gi | 897 CTGCTAGGGGGCCTCCTGCTCCATGGGGGTAGCTCTGGCCCCAGCCCCGGCCCCAGTGTG
                    50
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                                    70
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            380
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                            400
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LEX151 CCCCGCCTGCGGCTCTCCTACCGAGACCTCCTGTCTGCCAACCGCTCTGCCATCTTTCTG
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LEX151—GGCCCCCAGGGCTCCCTGAACCTCCAGGCCATGTACCTAGATGAGTACCGAGACCGCCTC
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LEX151 TTTCTGGGTGGCCTGGACGCCCTCTACTCTCTGCGGCTGGACCAGGCATGGCCAGATCCC
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	70	680	690	700	710	720	00020
LEX151					CTGTGCCCTCA		
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7	30	740	750	760	770	780	
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ai 897					::::::::: ATAGACGGGG		
3-1	3013113	520	530	540	550	560	570
0.1	- 0	0.60	0.70	000	000	000	
	50 - ሮሞሮ አርሞ(860 CCTGACTTCC	870 TGGGGCGAGA	088 Этартарано	890 TTCCGAAGTG	900 GAGGTCCTC	GCCA
	:::::	:::::::::	::::::::::	:::::::::	:::::::::		::::
gi 897	CTCACT				TTCCGAAGTG		
*		580	590	600	610	620	630
9:	10	920	930	940	950	960	
LEX151					GACCCCCGGT		
ai 897					GACCCCCGGT		
91 05 /	001010	640	650	660	670	680	690
97 T.EV151		980 ~~~~~~~~~~~~	990 Сталсалсал	1000	1010 GTGTACTTCT	1020 #C##C#CCC3	CACC
DDMIJI					:::::::::		
gi 897	CGGATC				GTGTACTTCT	TCTTCTCGGA	AGACG
		700.	710	720	730	740	750
103	30	1040	1050	1060	1070	1080	
					GTCAGCCGCG'		CTGC
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109		1100	1110	1120	1130	1140	~~~
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115	60	1160	1170	1180	1190	1200	
					GAGACCCACT		'AGAG
gi 897	AGGCTGG	TCTGCTCGG1 880	rGCCCGGCCC' 890	TGGTGGTGCC(900	GAGACCCACT 910	rtgaccagct 920	AGAG 930
				200	710	<i>72.</i> 0	930
121	0	1220	1230	1240	1250	1260	

·								
	LEX151					AGCCTCGAGG'		
	gi 897					::::::::::::::::::::::::::::::::::::::		
				330	300	3.0	500	,,,,
	12° LEX151		1280 CAGTGCCGT	1290 CGTTCCAGGGC		1310 TGTGTGTACC	1320 ACATGGCAGA	CATCTGG
	~:1007					:::::::::: TGTGTGTACC		
	g1 09/	ACCGI	1000	1010	1020	1030	1040	1050
	13.		1340			1370		
	LEX151					GGGCCTCAGC		
	ai 1897					::::::::: GGGCCTCAGC		
	9-102,	0001	1060	1070	1080	1090	1100	1110
	139	90	1400	1410	1420	1430	1440	
	LEX151	GGGGG	CAAGGTGCC	CTTCCCTCGC	CCTGGCGTG	TGCCCCAGCAA	GATGACCGC	ACAGCCA
						: : : : : : : : : :		
	g1 897	GGGGG	CAAGGTGCC 1120	TTCCCTCGC	CCTGGCGTG	rgccccagcaa 1150		
			1120	1130	1140	1120	1160	1170
	145	. •	1460		1480		1500	
	LEX151					GATGAGGTGCT		
	ai 1897					:::::::: GATGAGGTGCT		
	gijosi	GGACG	1180		1200	1210	1220	1230
	151	.0	1520	1530	1540	1550	1560	
	LEX151	CACCC	CCTCATGTT			CATGGCCGCCC		CAAGACC
		:::::	:::::::	:::::::::	: : : : : : : : :		:::::::	::::::
	g1 897	CACCCC	CCTCATGTT 1240	1250	1260	CATGGCCGCCC 1270	TGTCCTTGT	1290
٠	157	0	1580	1590	1600	1610	1620	
	LEX151	CACCTO	GCCCAGCA			ACCGCGTGGA	GGCAGAGGA'	rgggacc
						::::::::		
	g1 897	CACCTO	GCCCAGCA	GCTACACCAG 1310	ATCGTGGTGG	ACCGCGTGGA	GGCAGAGGA' 1340	rgggacc 1350
			1300.	1310	1320	1330	1340	1350
	163		1640	1650	1660	1670	1680	
						CTGTGCTCAA		
						CTGTGCTCAA		
	91/05/	INCONI	1360	1370	1380	1390	1400	1410
	169		1700	1710	1720	1730	1740	
						TGGAGGAGCT		
						TGGAGGAGCT		
			1420	1430	1440	1450	1460	1470
	175	0	1760	1770	1780	1790	1800	
						AAAGGCAAATO		
		CCAACA				::::::::: AAAGGCAAAT(1510		
	1810)	1820	1830	1840	1850	1860	

LEX151 C	GGCTGGGTGTGGC	CCAGCTGCGG	CTGCACCAA	GTGAGACTT	ACGGCACTGC	CTGTGCA
	:::::::::::::::::::::::::::::::::::::::					
g1 89/ C	GGCTGGGTGTGGC0 1540		CTGCACCAAT		ACGGCACTGC 1580	CTGTGCA 1590
				23.0	1500	1330
1870	1880 AGTGCTGCCTGGCO		1900	1910	1920	~~· ~~· ~
	3G1GC1GCC1GGCC					
	AGTGCTGCCTGGCC	CCGGGACCCA	TACTGTGCCT			
	1600	1610	1620	1630	1640	1650
1930	1940	1950	1960	1970	1980	
LEX151 CO	CCCCAGCCTTGGC	CAAGCGCCGG	TTCCGCCGGC	AGGACATCC	GCACGGCAA	CCCTGCC
~: 1007 CC	::::::::::::::::::::::::::::::::::::::	::::::::		:::::::::	::::::::	::::::
g1 897 CG	GCCCCAGCCTTGGC 1660	1670		1690	GCACGGCAA	1710
				1000	2700	1710
1990	2000		2020	2030	2040	
	GCAGTGCCTGGGC					
	GCAGTGCCTGGGC					
	1720	1730	1740	1750	1760	1770
2050	2060	2070	2080	2090	2100	
LEX151 GT	CTACGGCACGGAG					CARGCT
	:::::::::::::::::::::::::::::::::::::::					
g1 897 GT	CTACGGCACGGAG 1780		ACCTTCCTGG. 1800		CAAGTCTCCC 1820	
	1,700	1750	1000	1810	1020	1830
2110	2120	2130	2140	2150	2160	
	TGTGCGCTGGCTC' ::::::::::					
gi 897 GC	TGTGCGCTGGCTC'	TTGCAGAGGC	CAGGGGATG	AGGGGCCTGA	CCAGGTGAAG	ACGGAC
	1840	1850	1860	1870	1880	1890
2170	2180	2190	2200	. 2210	2220	
	GCGAGTCTTGCAC	ACGGAGCGGG	GGCTGCTGTT	CCGCAGGCT'		GATGCG
::	: : : : : : : : : : : : : :	: : : : : : : : :	:::::::::		: : : : : : : : :	:::::
gilaa/ GAG	GCGAGTCTTGCAC 1900		GGCTGCTGT7	CCGCAGGCT' 1930	FAGCCGTTTC 1940	GATGCG 1950
		1310	1320	1550	1740	1930
2230	2240	2250	2260	2270	2280	
:::	CACCTACACCTGCA	ACCACTCTGG	AGCATGGCTT	CTCCCAGAC	rgtggtccgc	CTGGCT
gi 897 GGC	CACCTACACCTGC	ACCACTCTGG	AGCATGGCTT	CTCCCAGACT	TGTGGTCCGC	CTGGCT
	1960	1970	1980	1990	2000	2010
2290	2300	2310	2320	2330	2340	
LEX151 CTC	GTGGTGATTGTGG	CCTCACAGC	TGGACAACCT	GTTCCCTCC	GAGCCAAAG	CCAGAG
:::	CTCCCTCC TTCCTCC	: : : : : : : : :	::::::::::	:::::::::::::::::::::::::::::::::::::::	::::::::	
91 (097 CTG	GTGGTGATTGTGG 2020	CCTCACAGC	TGGACAACCT 2040	GTTCCCTCCG 2050	GAGCCAAAG(2060	CCAGAG 2070
		2030	2040	2030	2000	2070
2350	2360	2370	2380	2390	2400	_
PEVIDI GAG	CCCCCAGCCCGGG	GAGGCCTGG	CTTCCACCCC	ACCCAAGGCC	TGGTACAAG	GACATC
gi 897 GAG	CCCCCAGCCCGGG	GAGGCCTGG	CTTCCACCCC	ACCCAAGGCC	TGGTACAAG	GACATC
		2090	2100	2110	2120	2130
2410	2420	2430	2440	2450	2460	
	-	= =		~ 130	2400	

```
LEX151 CTGCAGCTCATTGGCTTCGCCAACCTGCCCCGGGTGGATGAGTACTGTGAGCGCGTGTGG
      gi | 897 CTGCAGCTCATTGGCTTCGCCAACCTGCCCCGGGTGGATGAGTACTGTGAGCGCGTGTGG
                  2150
                          2160
                                  2170
           2480
                   2490
                           2500
   2470
                                   2510
                                           2520
LEX151 TGCAGGGCCACCACGGATGCTCAGGCTGCTTCCGGAGCCGGAGCCGGGCCAAGCAGGCC
      gi | 897 TGCAGGGGCACCACGGAATGCTCAGGCTGCTTCCGGAGCCGGAGCCGGGGCAAGCAGGCC
                  2210
                          2220
                                  2230
   2530
           2540
                   2550
                           2560
                                   2570
                                          2580
LEX151 AGGGGCAAGAGCTGGGCAGGGCTGGAGCTAGGCAAGAAGATGAAGAGCCGGGTGCATGCC
      gi | 897 AGGGGCAAGAGCTGGGCAGGGCTAGGCAAGAAGATGAAGAGCCGGGTGCATGCC
          2260
                  2270
                          2280
                                 2290
                                         2300
           2600
                   2610
                          2620
LEX151 GAGCACAATCGGACGCCCCGGGAGGTGGAGGCCACGTAG
      gi | 897 GAGCACAATCGGACGCCCCGGGAGGTGGAGGCCACGTAGAAGGGGGCAGAGGAGGGGTGG
          2320
                  2330
                          2340
                                  2350
2380
                  2390
                          2400
                                 2410
>>gi|8978201|dbj|AB029496.1| Homo sapiens mRNA for semap (4700 nt)
rev-comp initn: 83 init1: 83 opt: 95
67.105% identity in 76 nt overlap (119-46:407-475)
           140
                  130
                          120
LEX15- GCGGGAAGAGGGGCGGAGGAGAGAGGAGGCCTGGGGCCTTGCCGTCCACCTGCCGCTTCT
                             gi|897 ACAACCGGACCCACCTGCTAGCCTGTGGCACTGGGGCCCTTCCAGCCCACCTGTGCC--CT
              390
                      400
                             410
                                     420
                                             430
           80
                    70
                             60
                                     50
                                            40
LEX15- CCTTCCACCTTGTTGGCC-CAGTGCAG-GCTTTTGTGCCACACTGGCCAGCTCCCCATTG
     gi|897 CATCACA----GTTGGCCACCGTGGGGAGCATGTGCTCCAC-CTGGAGCCTGGCAGTGTG
                  450
                          460
     30 20 10
LEX15- GGAAGACCTTCCCAGCTAGGGCACAGGCCAT
gi|897 GAAAGTGGCCGGGGGCGGTGCCCTCACGAGCCCAGCCGTCCCTTTGCCAGCACCTTCATA
   490
           500
                   510
                           520
                                   530
```

```
2628 residues in 1 query sequences
4700 residues in 1 library sequences
Scomplib [version 3.3t05 March 30, 2000]
start: Fri Sep 19 13:50:44 2003 done: Fri Sep 19 13:50:45 2003
Scan time: 0.117 Display time: 0.133
```

Function used was FASTA

Exhibit BB

Home Paracel BLAST Results Help MEGABLAST 1.2.3-Paracel [2001-11-20] Reference: Zheng Zhang, Scott Schwartz, Lukas Wagner, and Webb Miller (2000), "A greedy algorithm for aligning DNA sequences", J Comput Biol 2000; 7(1-2):203-14. Database: Homo_sapiens.latestgp.fa 26,679 sequences; 200,800,637,119 total letters Query= 1 (2629 letters) Score Ε Sequences producing significant alignments: Value (bits) AC006208.3.1.123943 940 0.0 AC000063.1.1.34478 72 2e-09 AC079799.7.1.172495 54 5e-04 >AC006208.3.1.123943 Length = 123943Score = 940 bits (474), Expect = 0.0Identities = 474/474 (100%) Strand = Plus / Minus Query: 2156 caggtgaagacgagcgagtcttgcacacggagcggggctgctgttccgcaggctt 2215 Sbjct: 44516 caggtgaagacggacgagtcttgcacacggagcgggggctgctgttccgcaggctt 44457 Query: 2216 agccgtttcgatgcgggcacctacacctgcaccactctggagcatggcttctcccagact 2275 Sbjct: 44456 agccgtttcgatgcgggcacctacacctgcaccactctggagcatggcttctcccagact 44397 gtggtccgcctggctctggtggtgattgtggcctcacagctggacaacctgttccctccg 2335 Sbjct: 44396 gtggtccgcctggctctggtggtgattgtggcctcacagctggacaacctgttccctccg 44337 Query: 2336 gagccaaagccagaggagccccagcccggggaggcctggcttccacccaacccaaggcc 2395 Query: 2396 tggtacaaggacatcctgcagctcattggcttcgccaacctgccccgggtggatgagtac 2455

tgtgagcgcgtgtggtgcaggggcaccacggaatgctcaggctgcttccggagccggagc 2515

Sbjct: 44276 tggtacaaggacatcctgcagctcattggcttcgccaacctgccccgggtggatgagtac 44217

Sbjct: 44216 tgtgagcgcgtgtggtgcaggggcaccacggaatgctcaggctgcttccggagccggagc 44157

Query: 2456

```
Query: 2516 cggggcaagcaggccaggggcaagagctgggcagggctggagctaggcaagaagatgaag 2575
          Sbjct: 44156 cggggcaagcaggccaggggcaagagctgggcagggctggagctaggcaagaagatgaag 44097
Query: 2576 agccgggtgcatgccgagcacaatcggacgccccgggaggtggaggccacgtag 2629
          Sbjct: 44096 agccgggtgcatgccgagcacaatcggacgccccgggaggtggaggccacgtag 44043
 Score = 781 bits (394), Expect = 0.0
 Identities = 394/394 (100%)
 Strand = Plus / Minus
          atggcctgtgccctagctgggaaggtcttcccaatggggagctggccagtgtggcacaaa 61
Query: 2
          Sbjct: 53746 atggcctgtgccctagctgggaaggtcttcccaatggggagctggccagtgtggcacaaa 53687
          agcctgcactgggccaacaaggtggaaggaggaagggcaggtggacggcaaggccccagc 121
Query: 62
          Sbjct: 53686 agcctgcactgggccaacaaggtggaaggagaagcggcaggtggacggcaaggccccagc 53627
Query: 122
          ctccttctctcctccgccctcttcccgcccaggactgggtggagccactgccttataag 181
          Sbjct: 53626 ctccttctctctccccccctcttcccgcccaggactgggtggagccactgccttataag 53567
Query: 182
          tggtggcctggtggcagcagagcaaactacaaccggcggccagcgggaccagagggcggc 241
          Sbjct: 53566 tggtggcctggtggcagcagagcaaactacaaccggcggccagcgggaccagagggcggc 53507
Query: 242
          tetgeaggeaggeggeageggtgeeeteagtteeeeageatggeeeeeteggeetgggee 301
          Sbjct: 53506 tctgcaggcaggcggcagcggtgccctcagttccccagcatggccccctcggcctgggcc 53447
Query: 302
          atttgctggctgctagggggcctcctgctccatgggggtagctctggccccagccccggc 361
          Sbjct: 53446 atttgctggctgctagggggcctcctgctccatggggggtagctctggccccagccccggc 53387
Query: 362
          cccagtgtgccccgcctgcggctctcctaccgag 395
          Sbjct: 53386 cccagtgtgccccgcctgcggctctcctaccgag 53353
Score = 462 \text{ bits } (233), \text{ Expect = } e-127
Identities = 233/233 (100%)
Strand = Plus / Minus
Query: 1423
          gtgccccagcaagatgaccgcacagccaggacggccttttggcagcaccaaggactaccc 1482
```

```
Sbjct: 48539 gtgccccagcaagatgaccgcacagccaggacggccttttggcagcaccaaggactaccc 48480
 Query: 1483 agatgaggtgctgcagtttgcccgagcccacccctcatgttctggcctgtgcggcctcg 1542
           Sbjct: 48479 agatgaggtgctgcagtttgcccgagcccacccctcatgttctggcctgtgcggcctcg 48420
 Query: 1543 acatggccgcctgtccttgtcaagacccacctggcccagcagctacaccagatcgtggt 1602
           Sbjct: 48419 acatggccgccctgtccttgtcaagacccacctggcccagcagctacaccagatcgtggt 48360
 Query: 1603 ggaccgcgtggaggcagaggatgggacctacgatgtcattttcctggggactg 1655
           Sbjct: 48359 ggaccgcgtggaggcagaggatgggacctacgatgtcattttcctggggactg 48307
  Score = 456 \text{ bits } (230), Expect = e-125
  Identities = 230/230 (100%)
  Strand = Plus / Minus
 Query: 1789 gcaaatgctatacgtgggctctcggctgggtgtggcccagctgcggctgcaccaatgtga 1848
           Sbjct: 46640 gcaaatgctatacgtgggctctcggctgggtgtggcccagctgcggctgcaccaatgtga 46581
 Query: 1849
           gacttacggcactgcctgtgcagagtgctgcctggcccgggacccatactgtgcctggga 1908
           Sbjct: 46580 gacttacggcactgcctgtgcagagtgctgcctggcccgggacccatactgtgcctggga 46521
Query: 1909
           tggtgcctcctgtacccactaccgcccagccttggcaagcgccggttccgccggcagga 1968
           Sbjct: 46520 tggtgcctcctgtacccactaccgccccagccttggcaagcgccggttccgccggcagga 46461
Query: 1969 catccggcacggcaaccctgccctgcagtgcctgggccagagccaggaag 2018
Sbjct: 46460 catccggcacggcaaccctgccctgcagtgcctgggccagagccaggaag 46411
 Score = 327 bits (165), Expect = 2e-86
 Identities = 165/165 (100%)
 Strand = Plus / Minus
```

ctactctctgcggctggaccaggcatggccagatccccgggaggt 558 Query: 514

Sbjct: 51229 ctactctctgcggctggaccaggcatggccagatccccgggaggt 51185

Score = 294 bits (148), Expect = 3e-76

Identities = 148/148 (100%)

Strand = Plus / Minus

Query: 1276 cagtgccgtgttccagggcttcgccgtctgtgtgtaccacatggcagacatctgggaggt 1335

Sbjct: 48964 cagtgccgtgttccagggcttcgccgtctgtgtgtaccacatggcagacatctgggaggt 48905

Query: 1336 tttcaacgggccctttgcccaccgagatgggcctcagcaccagtgggggccctatggggg 1395

Sbjct: 48904 tttcaacgggccctttgcccaccgagatgggcctcagcaccagtgggggccctatggggg 48845

Query: 1396 caaggtgcccttccctcgccctggcgtg 1423

Sbjct: 48844 caaggtgcccttccctcgccctggcgtg 48817

Score = 292 bits (147), Expect = 1e-75

Identities = 147/147 (100%)

Strand = Plus / Minus

gaccccggtttgtgatggccgcccggatccctgagaactctgaccaggacaatgacaag 1006 Query: 947

Sbjct: 49850 gacccccggtttgtgatggccgcccggatccctgagaactctgaccaggacaatgacaag 49791

gtgtacttcttcttctcggagacggtcccctcgcccgatggtggctcgaaccatgtcact 1066 Query: 1007

Sbjct: 49790 gtgtacttettetteteggagaeggteeeetegeeegatggtggetegaaceatgteaet 49731

gtcagccgcgtgggccgcgtctgcgtg 1093 Query: 1067

Sbjct: 49730 gtcagccgcgtgggccgcgtctgcgtg 49704

Score = 286 bits (144), Expect = 6e-74

Identities = 145/146 (99%)

Strand = Plus / Minus

Query: 2017 agaagaggcagtgggacttgtggcagccaccatggtctacggcacggagcacaatagcac 2076

Sbjct: 46108 agaagaggcagtgggacttgtggcagccaccatggtctacggcacggagcacaatagcac 46049

Query: 2077 cttcctggagtgcctgcccaagtctccccargctgctgtgcgctggctcttgcagaggcc 2136

Sbjct: 46048 cttcctggagtgcctgcccaagtctccccaggctgctgtgcgctggctcttgcagaggcc 45989

Query: 2137 aggggatgaggggcctgaccaggtga 2162

Score = 240 bits (121), Expect = 3e-60

Identities = 121/121 (100%)

Strand = Plus / Minus

Query: 619 gacagagtgcgccaacttcgtgcgggtgctacagcctcacaaccggacccacctgctagc 678

Sbjct: 50745 gacagagtgcgccaacttcgtgcgggtgctacagcctcacaaccggacccacctgctagc 50686

Query: 679 ctgtggcactggggccttccagcccacctgtgccctcatcacagttggccaccgtgggga 738

Sbjct: 50685 ctgtggcactggggccttccagcccacctgtgccctcatcacagttggccaccgtgggga 50626

Query: 739 g 739

Sbjct: 50625 g 50625

Score = 236 bits (119), Expect = 5e-59

Identities = 119/119 (100%)

Strand = Plus / Minus

Query: 829 agacggggagctgtacacgggtctcactgctgacttcctgggggcgagaggccatgatctt 888

Sbjct: 50132 agacggggagctgtacacgggtctcactgctgacttcctggggcgagaggccatgatctt 50073

Query: 889 ccgaagtggaggtcctcggccagctctgcgttccgactctgaccagagtctcttgcacg 947

Sbjct: 50072 ccgaagtggaggtcctcggccagctctgcgttccgactctgaccagagtctcttgcacg 50014

Score = 230 bits (116), Expect = 3e-57

Identities = 116/116 (100%)

Strand = Plus / Minus

Query: 1093 gaatgatgctgggggccagcgggtgctggtgaacaaatggagcactttcctcaaggccag 1152

Sbjct: 49489 gaatgatgctgggggccagcgggtgctggtgaacaaatggagcactttcctcaaggccag 49430

Query: 1153 gctggtctgctcggtgcccggccctggtggtgccgagacccactttgaccagctag 1208

Sbjct: 49429 gctggtctgctcggtgcccggccctggtggtgccgagacccactttgaccagctag 49374

Score = 188 bits (95), Expect = 1e-44Identities = 95/95 (100%) Strand = Plus / Minus Query: 1715 gaagtggttctggaggagctccaggtgtttaaggt 1749 Sbjct: 48152 gaagtggttctggaggagctccaggtgtttaaggt 48118 Score = 184 bits (93), Expect = 2e-43Identities = 93/93 (100%) Strand = Plus / Minus Query: 738 Query: 798 agcccagccgtccctttgccagcaccttcatag 830 111111111111111111111111111111111111 Sbjct: 50291 agcccagccgtccctttgccagcaccttcatag 50259 Score = 143 bits (72), Expect = 6e-31Identities = 72/72 (100%) Strand = Plus / Minus Query: 1207 agaggatgttcctgctgtggcccaaggccgggaagagcctcgaggtgtacgcgctgtt 1266 Sbjct: 49265 agaggatgtgttcctgctgtggcccaaggccgggaagagcctcgaggtgtacgcgctgtt 49206

Query: 1267 cagcaccgtcag 1278

Sbjct: 49205 cagcaccgtcag 49194

Score = 129 bits (65), Expect = 9e-27Identities = 65/65 (100%) Strand = Plus / Minus

aggtcctgtggccaccgcagccaggacagagggaggagtgtgttcgaaagggaagagatc 614 Sbjct: 51063 aggtcctgtggccaccgcagccaggacagagggaggagtgtgttcgaaagggaagagatc 51004 Query: 615 ctttg 619 11111

Sbjct: 51003 ctttg 50999

Score = 87.8 bits (44), Expect = 3e-14Identities = 44/44 (100%) Strand = Plus / Minus

Query: 1746 aggtgccaacacctatcaccgaaatggagatctctgtcaaaagg 1789

Sbjct: 47403 aggtgccaacacctatcaccgaaatggagatctctgtcaaaagg 47360

>AC000063.1.1.34478 Length = 34478

Score = 71.9 bits (36), Expect = 2e-09Identities = 48/52 (92%) Strand = Plus / Minus

Query: 1860 ctgcctgtgcagagtgctgcctggcccgggacccatactgtgcctgggatgg 1911 Sbjct: 5711 ctgcctgtgctgactgctgccttgcccgggacccttactgtgcctgggatgg 5660

>AC079799.7.1.172495 Length = 172495

Score = 54.0 bits (27), Expect = 5e-04Identities = 42/47 (89%) Strand = Plus / Minus

Query: 1865 tgtgcagagtgctgcctggcccgggacccatactgtgcctgggatgg 1911

Sbjct: 151014 tgtgctgactgctggctcgagacccttactgtgcctgggatgg 150968

Database: Homo_sapiens.latestgp.fa Posted date: Jul 8, 2003 12:51 PM

Number of letters in database: 200,800,637,119

Number of sequences in database: 26,679

Lambda K 1.37 0.711 1.31

Gapped Lambda 1.37 0.711 1.31

Matrix: blastn matrix:1 -3

Gap Penalties: Existence: 0, Extension: 0

```
Number of Hits to DB: 0
length of query: 5260
length of database: 200,800,637,119
effective HSP length: 22
effective length of query: 2607
effective search space used:
T: 0
A: 0
X1: 0 ( 0.0 bits)
X2: 20 (39.7 bits)
S1: 12 (24.3 bits)
S2: 24 (48.1 bits)
```